

CONCLUSIONS Tolterodine inhibited hERG channel in open channel state-dependent and concentration-dependent manner, and was a potent inhibitor of hERG channel expressed in *Xenopus* oocytes. Two aromatic residues: Y652 and F656, on the inner (S6) helix, seemed to be critical for high-affinity of tolterodine binding to hERG channel.

GW26-e0246

Metformin Activate AMPK, Inhibit GRP78 in liver and improve Insulin Sensitivity in Polycystic Ovarian Syndrome Rats

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OBJECTIVES To investigate the effects of metformin on insulin sensitivity and possible mechanism in rats with polycystic ovarian syndrome (PCOS).

METHODS PCOS rat model was induced by subcutaneous injecting dehydroepiandrosterone (0.6mg·kg⁻¹·d⁻¹) up to 20 days and then divided randomly into PCOS and metformin group (metformin 140mg·kg⁻¹·d⁻¹ for 15 days). Blood were collected to test free glucose and insulin levels before and after metformin intervention. Liver tissues were collected to test triglyceride (TG) content and protein expression.

RESULTS PCOS rats exhibit insulin resistance and metformin treatment improve insulin sensitivity in PCOS rats. TG levels, glucose regulated protein 78 (GRP78) and sterol regulatory element-binding protein -1c (SREBP-1c) protein expression in the liver of PCOS rats were higher than those of the controls, whereas phosphorylation adenosine monophosphate-activated protein kinase (P-AMPKα) protein expression was lower than that of the normal controls (p<0.05). After metformin treatment, TG levels, GRP78 and SREBP-1c protein expression in the liver of PCOS rats were significantly decreased (p<0.05) and P-AMPKα protein expression was increased to the level similar with that of normal controls.

CONCLUSIONS Metformin protect PCOS rats from insulin resistant and hepatocytic fat deposition largely through the effects on activating AMPK pathway and on inhibiting endoplasmic reticulum stress in liver.

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Effect of Jiashen prescription on left ventricular remodeling and inflammatory response at the early stage of myocardial infarction

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OBJECTIVES This study was designed to determine the effects of Jiashen prescription (JSP) on left ventricular remodeling and inflammatory response at the early stage of MI in rats.

METHODS MI was induced by the ligation of left anterior descending coronary artery in Sprague-Dawley rats. The rats were divided into five groups after 24 hours: sham-operated group; MI+vehicle group; JSP-3g (3g/kg/day) group; JSP-6g (6g/kg/day) group and losartan (10mg/kg/day) group. The left ventricular structure and function were measured by echocardiography at week 4 after MI. The infiltration of monocyte/macrophage in the myocardial tissue was evaluated by the use of immunohistochemical stain. The expression of intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) was determined using Western blot.

RESULTS Compared to MI+vehicle rats, JSP at the dose of 6 g/kg/day attenuated the increases in left ventricular end-diastolic dimension (8.8±0.5 vs. 7.1±0.3 mm, P<0.05) and left ventricular end-systolic dimension (7.1±0.6 vs. 4.4±0.2 mm, P<0.05), and the decreases in ejection fraction (43±6% vs. 74±1%, P<0.05) and fractional shortening (19±3% vs. 39±1%, P<0.05) at week 4 after MI. In addition, treatment with JSP at the dose of 6 g/kg/day inhibited the number of monocyte/macrophages (14.3±1.8 vs. 9.3±0.3, P<0.05) and expression of ICAM-1 and VCAM-1 compared to MI+vehicle rats at week 4 after MI (ICAM-1: 0.40±0.13 vs. 0.81±0.19 GAPDH arbitrary units; VCAM-1: 0.23±0.05 vs. 0.58±0.02 GAPDH arbitrary units, P<0.05). Losartan treatment has a similar results with JSP at the dose of 6 g/kg/day.

CONCLUSIONS Our studies showed that JSP administered after MI improved cardiac function, and inhibited left ventricular dilatation. The results were associated with the inhibition of monocyte/macrophage infiltration and the decreased production of inflammatory

mediators. Our data suggest that JSP improves left ventricular remodeling possibly via inhibiting inflammatory response at the early stage of MI. [This work was supported by a grant from the National Natural Science Foundation of China (No. 81173410) to M.J.Z.].

GW26-e1063

Effects of Danqi Pill on altered global gene expression pattern induced by myocardial ischemia

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OBJECTIVES To systematically characterize altered gene expression pattern induced by myocardial ischemia (MI) in rat model and to investigate the effects of Danqi Pill (DQP) on global gene expression in the treatment of myocardial ischemia.

METHODS Myocardial ischemia rat model was induced by left anterior descending coronary artery ligation. Nine rats were randomly divided into sham-operated group, model group and DQP-treated group. At 28 days after treatment, cardiac function was evaluated by echocardiography. Heart tissues in infarct border zone were homogenized and total mRNA was extracted. Global mRNA expression was measured using Illumina's digital gene expression profiling method. Differentially expressed genes between model group and sham operated group were investigated and differentially expressed genes between DQP group and ischemia model group were also analyzed. The gene ontology (GO) enrichment analysis and pathway analysis of all differentially expressed genes were carried out using DAVID Functional Annotation Tool.

RESULTS Ejection Fraction (EF) and fractional shortening (FS) of rats in model group were significantly lower than those of sham-operated group, indicating that MI model was successfully induced. In DQP group, EF and FS increased compared with those in model group. We detected and quantified 8062 genes in these three groups. Compared with sham-operated group, expressions of 360 genes were up-regulated and 179 genes were down-regulated in model group. GO and pathway analysis showed that up-regulated genes were enriched in extracellular matrix organization, response to wounding and defense response pathways, indicating changes in cardiac hypertrophy and remodeling. Down-regulated genes were enriched in fatty acid metabolism, pyruvate metabolism, PPAR signaling pathways, etc. This indicated that energy metabolism disorders occurred in MI. In DQP group, expressions of genes in the altered pathways were regulated back towards normal levels. DQP reversed expression of 90% of the 539 differentially expressed genes in model group. For example, genes involved in remodeling process, such as collagen I and III, connective tissue growth factor and MMP2, were down-regulated by DQP. Genes involved in energy metabolisms, such as acyl-coenzyme A dehydrogenase, mitofusion1 and sirtuins5, were up-regulated by DQP. DQP also regulated the expressions of 12 deregulated transcription factors, including adipocyte enhancer-binding protein 1, which mediates inflammation; CCAAT/Enhancer binding protein delta, which plays roles in lipid metabolism and nuclear factor of activated T-cell 4, which regulates mitochondrial function and promotes cardiac fibrosis.

CONCLUSIONS Danqi pill exerts cardio-protective effect by regulating global gene expression pattern in ischemic heart tissue. It could attenuate fibrosis by down-regulating genes involved in extracellular matrix organization and improve cardiac metabolism by up-regulating genes involved in lipid metabolism and energy production pathways.

GW26-e1309

Effects of rosiglitazone on the levels of high mobility group protein box1 from cultured human umbilical vein endothelial cells induced by LPS

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OBJECTIVES To investigate the expression of HMGB1 on LPS-induced HUVECs in vitro and the effect of rosiglitazone on the expression of HMGB1.

METHODS Cultured HUVECs in vitro at passage 3 to 7 were used for experiment. There were three groups: (1) control group; (2) LPS groups; HUVECs were incubated with 1mg/L LPS for different periods to measure cytoactive of HUVECs by MTT colorimetric assay and HMGB1 expression (by ELISA) at 6h, 12h, 24h. Then observe the effect of different concentration rosiglitazone (RSG) on the cell proliferating vitality and HMGB1 expression compared with control group and LPS groups by ELISA.